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Model Based Economic Evaluations of Diagnostic Point of Care Tests Are Rarely Fit for Purpose

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Abstract

Objective

Linked evidence models are recommended to predict health benefits and cost-effectiveness of diagnostic tests. We considered how published models accounted for changes in patient pathways that occur with point of care tests (POCTs), and their impact of on patient health and costs.

Study Design and Setting

Model based evaluations of diagnostic POCTs published from 2004-2017 were identified from searching six databases. For each model we assessed the outcomes considered, and whether reduced time to diagnosis and increased access to testing affected patient health and costs.

Results

Seventy-four model based evaluations were included: 95% incorporated evidence on test accuracy, but 34% only assessed intermediate outcomes such as rates of correct diagnosis. Of 54 models where POCTs reduced testing time, 39% addressed the economic and 37% the health benefits of faster diagnosis. No model considered differences in access to tests.

Conclusions

Many models fail to capture the effects of POCTs in increasing access, advancing speed of diagnosis and treatment, reducing anxiety and the associated costs. Many only consider the impact of testing from changes in accuracy. Ensuring models incorporate changes in patient pathways from faster and more accessible testing will lead to economic evaluations that better reflect the impact of POCTs.

Keywords:

Diagnostic test; post of care test; decision model; clinical pathway; health economic model

What is new?

- Point of care tests have the potential to speed up decision making, enabling patients to access appropriate treatment faster and reduce anxiety waiting for results.
- Point of care tests can be undertaken in different settings allowing broader access to testing.
- Published model based economic models do not always capture the relevant patient and economic benefits of point of care tests, meaning that the conclusions from these models may not always be valid.
- We propose a checklist of considerations that should be made when developing models to evaluate the health economic impact of a POCT.
- Future studies that focus on the clinical and economic evaluation of POCTs should ensure that the specific characteristics of these tests are incorporated in the analysis.

1 Introduction

The decision to use a diagnostic test ideally should be based on evidence that it leads to better patient outcomes (1), and that improvements from testing are worth any additional costs involved. However, there are many logistical obstacles in directly evaluating the impact of tests on patient outcomes and their associated cost-effectiveness. There is a dearth of trials which randomly allocate participants between alternative testing strategies, evaluate resource use arising from testing and subsequent interventions, and compare final outcomes at the end of the health care episode (2). Where they do exist, they are often underpowered to detect differences in outcomes, potentially biased, and there are challenges in using their results to inform practice due to lack of standardization and detail about the test-treatment strategies used (3, 4).

Decision models provide an alternative approach to evaluate the likely effectiveness and cost-effectiveness of diagnostic tests. So called *linked evidence* models combine evidence on the performance of each test with evidence of the effectiveness of interventions to predict outcomes for each test-treat strategy. They can be used where there is no suitable evidence provided by randomised controlled trials (RCTs), and are recommended and routinely used by technology assessment organisations included the National Institute for Health and Care Excellence (NICE) in the UK (5) and the Agency for Healthcare Research and Quality (AHRQ) in the US (6). In their simplest form, models are constructed by estimating the proportions of true positives, true negatives, false positives and false negatives for each test strategy and assigning likely resource use and outcomes according to the disease state, and whether individuals receive appropriate effective treatment (dependent on whether the diagnosis is correct). A simplifying assumption is often made, that the management of each patient is determined entirely by the test result obtained and both clinicians and patients follow through with the recommended treatment. Outcomes such as quality adjusted life years (QALYs) are used to capture health benefits, as these allow comparisons of cost-effectiveness to be made for interventions across different settings (7). They also incorporate the unintended harm (8) and adverse events from unnecessary treatments following a false positive result, or the impact of continuing to suffer from a disease following a false negative test result (9).

In recent years there has been substantial investment in the development and provision of point of care tests (POCTs, also known as rapid tests or near patient tests) that can be conducted in close proximity (both in time and in setting) to a patient (10). Examples include nucleic acid amplification tests (NAATs) to diagnose tuberculosis (11) and immunochromatographic tests (ICT) for the diagnosis of influenza (12).

POCTs have the potential to revolutionize care pathways as they produce results more quickly than their laboratory counterparts, often allowing patient management to be determined in the same consultation when the test is deployed. This may shorten health care episodes through removing the time spent waiting for a diagnosis before any intervention can commence, and has associated economic benefits in terms of a reduction in length of hospital stay, repeat hospital admissions and clinic visits, and reductions in the use of interventions for symptom control whilst test results are awaited (13, 14). Faster testing could also reduce the costs incurred by patients and carers that fall outside of the healthcare system (15) (societal costs), including productivity losses and transport costs. In some conditions, patient outcomes may also be improved by earlier testing, both by avoiding deterioration in health (and even death) whilst awaiting test results, or where earlier initiation of a treatment may enhance its effectiveness (10, 13). Patients may also experience a reduction in anxiety (16) caused by delays in waiting for test results and initiation of treatment. In the case of infectious diseases faster testing may reduce disease transmission (17).

POCTs may also change the setting in which testing is undertaken as they are more portable than their laboratory equivalents, facilitating their deployment in community or primary health care settings rather than in secondary care. This may facilitate testing in settings where tests were not previously available. Thus a further perceived benefit of the introduction of POCTs is to widen access with more individuals receiving testing, particularly in rural areas in low and middle income countries (LMICs).

The benefits of earlier diagnosis and wider access may mean introduction of a POCT may be cost-effective even if it is less accurate and more costly than current practice (18). However, creating a decision model that fully captures the benefits of a faster and more accessible test requires incorporation of information about the likely difference in the timing of diagnosis on resource use, the effectiveness of earlier treatment on patient outcomes, and differences in the size and characteristics of the cohorts being tested.

In this review we evaluated published model based economic evaluations of POCTs to assess how evaluations have considered the impact of test timing and access to testing alongside differences in accuracy associated with the introduction of POCTs.

2 Methods

We identified recent model based published economic evaluations of POCTs, assessed the structure of their models, the parameters that they include and their outcomes, to identify whether they have appropriately considered the impact and costs of using a POCT.

2.1 Search strategy

Published reports of model based economic evaluations of point of care diagnostic tests were identified by searching electronic databases. Medline, Embase and PsycINFO, CINAHL, NHS Economic Evaluation Database (NHS EED) and Health Economic Evaluation Database (HEED) were searched in October 2017. Search strategies were developed based on validated algorithms for identifying health economic evaluations (19) and strings were used for the identification of POCTs in the published literature. Supplementary searches were conducted based on technical terms or proprietary names of tests found in the original searches, and on the bibliographies of included studies. We restricted the search to English language articles published between 2004 and 2017 with the aim to understand methods currently used when conducting economic evaluations of POCT technologies. Search strategies are provided in the Appendix.

2.2 Inclusion Criteria

Evaluations were included if they used a model based approach, were reported in a published manuscript, considered patients presenting with a specific complaint, signs or symptoms, and where at least one strategy involved a POCT (defined as a test performed near the patient or treatment facility with a fast turnaround time and may lead to a change in patient management) (10). We also included evaluations of accelerated laboratory tests that claimed similar changes to testing timeframes. The review was not restricted to any specific clinical specialities. We focused on diagnostic tests, and thus excluded studies that considered monitoring and screening tests. We excluded models which focused entirely on estimating clinical impact and did not include any economic component.

2.3 Selection of Articles

Titles and abstracts were screened for inclusion by one reviewer. Full text copies were retrieved for articles meeting the inclusion criteria or those providing insufficient information in the abstract to determine their eligibility. A second reviewer independently assessed articles that still did not clearly satisfy the inclusion criteria. Excluded articles and reasons for their exclusion were documented.

2.4 Data Extraction, Analysis and Reporting

A data extraction form was developed and piloted on a selection of articles and modified accordingly. We extracted data to document the inclusion of test accuracy, impact of faster testing on patient outcomes, impact of faster testing on costs, the effectiveness measure, the perspective for the costs adopted, and difference in setting and participants included for each strategy. Data were extracted by one author and checked by a second. We report the proportions of economic evaluations that demonstrate each characteristic.

3 Results

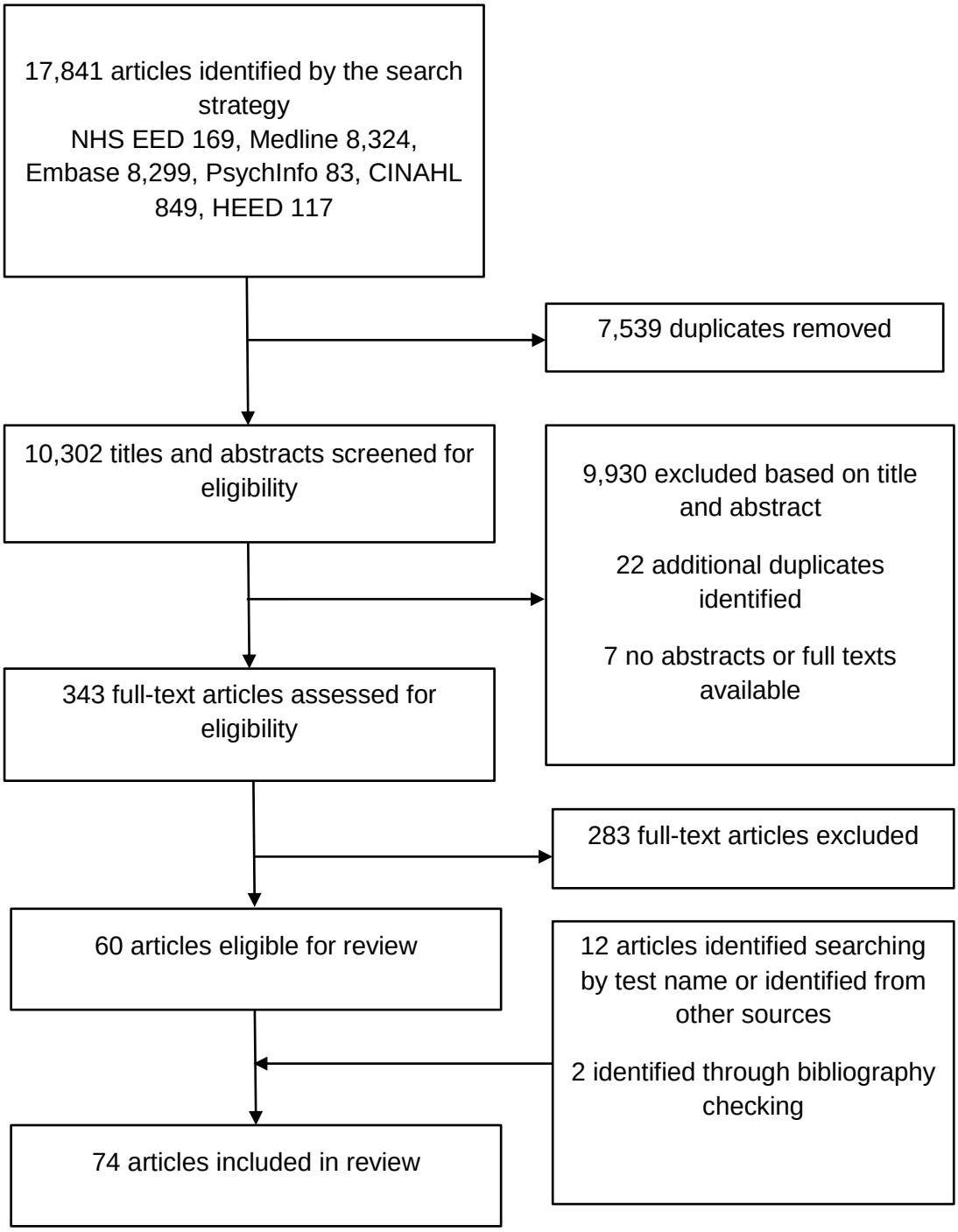

Figure 1 Flow Chart Demonstrating Selection of Papers

Our search identified 10,302 unique articles, of which 343 were considered potentially eligible and reviewed in detail. In total, 74 model based economic evaluations were identified as meeting our inclusion criteria (Figure 1). Evaluations covered diverse clinical conditions and were undertaken in primary care, hospital care and the community settings.

There were multiple evaluations of tests for the diagnosis of tuberculosis, malaria and influenza (Table 1).

Studies predominantly assessed the cost-effectiveness of implementing tests in Africa (31%), North America (24%) and Europe (22%). Twenty-four (32%) analyses were from the perspective of a LMIC country. Only one study evaluated a hypothetical test for tuberculosis (20), all others evaluated commercially available tests.

Table 1 Characteristics of Model Based Economic Evaluations

	Total (N=74)		**LMIC**			
Indication	N	(%*)	Yes (N=24)		No (N=50)	
			N	(%)	N	(%)
Tuberculosis	24	(32)	10	(42)	14	(28)
Malaria	13	(18)	11	(46)	2	(4)
Influenza	11	(15)	0	(0)	11	(22)
Pharyngitis	4	(5)	0	(0)	4	(8)
Pulmonary embolism	3	(4)	0	(0)	3	(6)
Deep vein thrombosis	3	(4)	0	(0)	3	(6)
Dyspepsia	3	(4)	0	(0)	3	(6)
Sepsis	2	(3)	1	(4)	1	(2)
Acute coronary syndrome	2	(3)	1	(4)	1	(2)
Respiratory tract infection	1	(1)	0	(0)	1	(2)
Acute myocardial infarction	1	(1)	0	(0)	1	(2)
C-difficile	1	(1)	0	(0)	1	(2)
Chlamydia and gonorrhoea	1	(1)	0	(0)	1	(2)
Conjunctivitis	1	(1)	0	(0)	1	(2)
Staphylococci infection	1	(1)	0	(0)	1	(2)
Staphylococcus aureus bacteraemia	1	(1)	0	(0)	1	(2)
Visceral leishmaniasis	1	(1)	1	(0)	0	(0)
Meningococcal disease	1	(1)	0	(0)	1	(2)

3.1 Effectiveness outcomes

The majority of models used measures of patient health in the primary analysis (65%): 22 (30%) reported Quality Adjusted Life Years (QALYs) (1 LMIC country), 11 (15%) Disability adjusted life years (DALYs) (9 LMIC countries), and a further 9 (12%) used mortality measures (6 LMIC countries) (Table 2). Twenty-five analyses (34%) (8 LMIC countries) focused on intermediate outcomes related to test results, diagnoses or treatment. Evaluations of tests for infectious diseases also considered markers of disease spread.

Table 2 Effectiveness Outcomes in Primary Analysis of Model Based Economic Evaluations

	Outcome used N=74	
	N	**%**
QALYs / QALDs /DALYs/ Quality adjusted survival	35	(47)
Deaths averted/life years saved or lost/death from target indication/cure without complications**/**symptom free days or years	13	(18)
Infections prevented*	1	(1)
Correct diagnosis/correct treatment/positive test**/**false positives/patients treated/ work productivity gained *	25	(34)

Quality adjusted life years (QALYs), Quality adjusted life days (QALDs), Disability adjusted life years (DALYs)
*Intermediate outcomes not demonstrating a direct health benefit

3.2 Cost perspective

The majority of the models that considered the impact of POCT on cost used a healthcare payer perspective (17/21) (21-38) and one model reported results using both a payer and societal perspective (39). The remaining three models reported a societal perspective only (40-42).

3.3 Test accuracy and diagnostic errors

Seventy of the 74 (95%) models considered test accuracy and 51 studies considered how varying test accuracy in sensitivity analysis would impact on the conclusions drawn from the analyses. Incorrect and failed tests can have implications for patient health and costs and 57 models addressed these issues. Unnecessary harms, such as adverse events from inappropriate treatment were estimated in 17 studies (23, 28, 31, 43-56), and the cost of treating a false positive or false negative patient in seven (33, 57-62). Three models adjusted mortality rates (63-65) and five cost utility analyses adjusted utilities due to the untreated disease state (24, 48, 54, 57, 61). The risk of transmission as a result of an incorrect

diagnosis was incorporated in four infectious disease models (60, 62, 66, 67), as was test failure (30, 34, 68, 69). The need for retesting after an incorrect result was considered in one study (70).

3.4 Effects of Faster Testing

The effects of timing of tests were judged of importance in 54 of the 74 models. The effects of diagnostic timing were not relevant in 20 studies (27%) (45, 46, 48-50, 54, 56, 67, 71-82), where the POCT could not affect the speed of treatment compared to the alternative strategy, for example, when the only comparator was presumptive treatment or no test. These were predominantly economic evaluations of malaria or tuberculosis tests.

Only 29 studies (20, 23, 24, 26-37, 41, 43, 44, 57, 58, 60, 62, 65, 69, 83-87) incorporated the aspect of time to diagnosis in the model. Thus, some aspect of the benefits of quicker test results were incorporated in just over half (54%; 29/54) of the models where it was of relevance (see Web Table 4 for description of how the 29 models incorporated time to diagnosis in terms of patient impact and/or costs).

Twenty models (37%) captured the impact of faster testing on patient outcomes: three by quicker resolution of disease (dyspepsia (43), pharyngitis (28, 84)); four through reductions in disease progression or reduced mortality (chlamydia and gonorrhoea progressing to pelvic inflammatory disease (35), mortality from sepsis (36), mortality from tuberculosis (24, 37)); seven from increases in the numbers starting treatment through reductions in loss to follow-up (all tuberculosis (23, 27, 29, 30, 34, 62, 69)); three from reductions in harms through reduced use of presumptive treatment (chlamydia and gonorrhoea (35), clostridium difficile infection (33), pharyngitis (44)), and one from reduced anxiety whilst waiting for results (chlamydia and gonorrhoea (35)). Two reduced QALYs to reflect the disutility of time in intensive care (36, 87).

Twenty-one models (39%) incorporated the impact of implementing a POCT on costs. Cost advantages for POCT arose from fewer visits to healthcare providers to receive results, less clinician time to conduct the test and shorter length of stay due to faster decision making and treatment initiation (23, 24, 26, 28-36, 41, 44, 60, 83, 84, 87). Reduced treatment or testing costs were observed as a result of avoiding presumptive treatment, additional tests and the need to treat disease which had progressed (24, 26, 27, 31, 33, 35, 37, 41, 43, 44, 87). Three models incorporated the time taken for testing, but it was unclear from the model descriptions how this would impact on costs or patient outcomes (20, 58, 65).

Figure 2 summarises how frequently the economic models considered faster testing in the analysis. ‘Included in model’ refers to any economic or patient impact parametrised in the model. Patient impact includes more effective earlier treatment, earlier treatment initiation and duration of illness reduced. Harms from unnecessary or inappropriate treatment are also incorporated, as are anxiety during the diagnostic delay and reduced disease progression.

Impact on operational costs refers to costs incurred when delivering treatment or testing procedures, such as clinical consultations or residing in hospital.

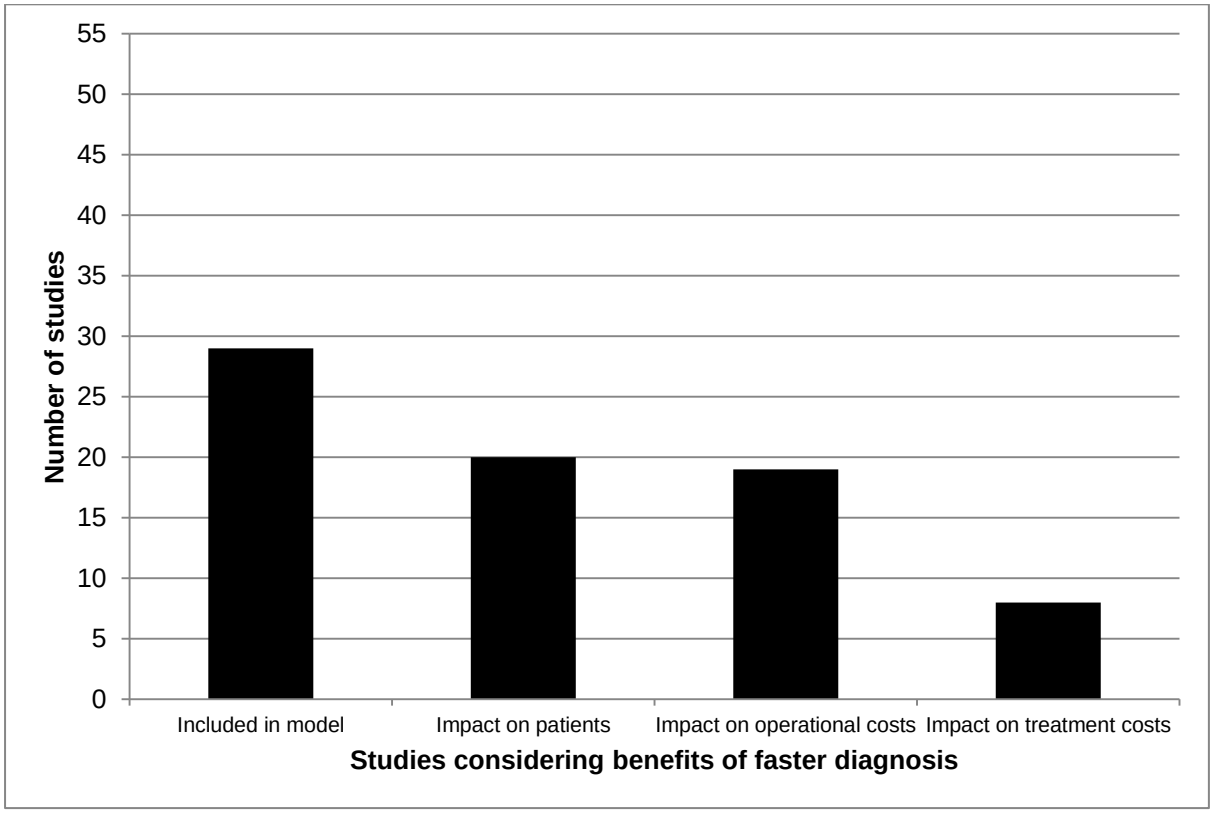

Figure 2 Frequency of the consideration of the effects of faster testing in the 54 model based economic evaluations where timing of tests differed between strategies compared (Included in model indicates that any difference in outcome or cost was considered).

3.5 Costs of the test-treatment pathway

Twenty-five studies included societal costs in the economic evaluation. In the case of influenza, antiviral treatment guided by rapid testing reduced symptom duration and productivity losses for patients or their carers were considered (45-48, 50, 67, 73), while in one tuberculosis study income loss was reduced as a result of fewer days of hospitalization waiting for smear/culture results (60). Other costs borne by patients and captured in the analyses included loss of income related to the duration of their clinic visit (40, 88) and travel costs (52, 60, 72, 89-91). The costing of productivity loss could enhance the cost-effectiveness of the POCTs, although in 85% of studies this was omitted. The majority of models included the cost of one course of treatment, such as antimalarials or antibiotics. Costs of treating complications from unresolved illnesses or adverse events were frequently included. A minority (5%) did not include any costs beyond the testing procedure (68, 92-94).

3.6 Access to testing

The introduction of a POCT changed the location of testing in eight models (26, 28, 41, 53, 72, 85, 89, 91) (Table 3). This was predominantly a move from secondary to primary care settings, with one model examined the provision of testing in a pharmacy setting (28).

Twenty-four analyses included a comparator arm of either presumptive treatment or no test. Of these, nine (46, 49, 50, 52, 76, 78, 79, 81, 82) did not include any slower testing method and therefore modelled a situation where testing was previously unavailable. In total, 11 (45.8%) economic evaluations conducted from the perspective of LMICs analysed the impact of introducing a test where current practice could result in a patient receiving no diagnostic test (49, 51-53, 71, 79, 81, 82, 89, 90, 95).

All models assumed that the same patient group would follow through each of the strategies considered; there was no allowance made in the POCT arms for inclusion of additional patients who access standard laboratory testing.

Table 3 Impact of POCT on Access to Testing

		Total (N=74)		**LMIC**			
		N	**(%)**	**Yes (N=24)**		**No (N=50)**	
				N	**(%)**	**N**	**(%)**
Change in geographical location (e.g. primary to secondary care)		8	(11)	3	(13)	5	(10)
Access to testing	Yes (slower test and no test/presumptive treatment)	15	(20)	6	(25)	9	(18)
	Yes (no test alternative)	9	(12)	5	(21)	4	(8)
Tested a different population		0	(0)	0		0	(0)

4. Discussion

Introduction of a POCT into a diagnostic pathway can substantially change diagnostic and treatment pathways, altering who is tested, when and where testing is done, when treatment can commence, and the health care resources, staff and equipment required. These changes impact on patient pathways, potentially changing patient outcomes.

In this review of recently published economic evaluations we found that many economic models evaluating POCT strategies failed to capture the key routes by which POCTs may create patient benefit and change resource use. In the models where there was a difference in timing of diagnosis between strategies, only 37% considered possible health benefits and 39% considered differences in resource use arising from reducing the time to diagnosis through switching to a faster test. There were no evaluations which considered how POCT availability and access may increase numbers undergoing testing.

In contrast, 95% of the reviewed models considered the impact of differences in accuracy, (higher than the 63% of cost-utility analyses of laboratory tests reviewed by Fang et al (8)). As point of care tests may have inferior accuracy compared to their laboratory based equivalents, it is important that any increase in false positive and false negative diagnoses through reduced accuracy is included in a decision model. Incorrect test results can have implications on costs, patient outcomes, affect disease transmission, and delay the diagnosis of other serious conditions, thus justifying their importance in analyses (96). However, where differences in accuracy are small, the greatest impact on outcomes and resource use is likely to occur from differences in the diagnostic and treatment pathways.

Around half the models reported utility based outcomes, such as the QALY, DALY and QALD. NICE (97) and The World Health Organisation Choosing Interventions that are Cost Effective (WHO-CHOICE) (98) project recommend the QALY and the DALY as effectiveness outcomes respectively as they allow incorporation of patient benefits and harms into a single metric. It is encouraging that these standardised measures are being used as the value of these tests can be assessed in comparable terms to treatments and other health technologies. However the appropriateness of an outcome predominantly composed of length of life for capturing benefits and harms in a testing situation is debatable. For example, how comparable are 10,000 patients waiting less time for a test result and increasing life expectancy of four patients by six months? Only one study addressed the psychological impact of waiting for test outcomes. When comparing a rapid test to a slower comparator, omitting a utility decrement or other methodology that captures anxiety experienced due to delay might not truly reflect the incremental benefit of a rapid test.

Intermediate outcomes related to tests or interventions were reported as the primary outcome in 32% of studies. In some circumstances these endpoints may be appropriate as surrogates for patient benefits, but they fail to consolidate the multiple ways in which tests impact on patients into a single measure. A minority of studies only considered the cost of the test and not the test-treatment pathway. As the intention of testing is to inform patient management and improve their health, these models fail to capture the true economic and health implications of the testing pathway.

Two thirds of models excluded costs incurred by patients, their carers and any impacts on productivity. The omission of these costs may be a consequence of adopting the perspective recommended by the target decision maker. In the UK, NICE (97) recommend that only costs borne by the NHS and personal social services are included. In contrast The Netherlands prescribe a societal perspective, to include costs of patient's time (leisure time and paid/unpaid work) and travel. Adhering to these guidelines limits the transferability of the results, yet may be an unavoidable consequence. Excluding societal costs may particularly undervalue POCT technologies as they typically provide savings to patients through reductions in time spend in contact with health services.

A previous evaluation considered models for evaluating POCT tests for tuberculosis (99). Challenges identified included uncertainties regarding transmission relative to time of diagnosis, treatment initiation and loss to follow-up. The ability of the health system to inform patients of test results and the timely initiation of treatment were described in some transmission and health system models, although not those evaluating cost-effectiveness (99). Similar to our findings; the cost-effectiveness models failed to model the full test treatment pathway and omitted patient incurred costs. As tuberculosis is a disease associated with poverty, patient costs could prove a barrier to testing. Drain et al proposed a specification (100) for an ideal evaluation of point of care tests for use in resource limited settings, suggesting a shift in emphasis from test accuracy to outcomes such as time to treatment initiation or patient notification rate. In resource limited settings clinical benefit from expediting decision making may be of greater value than test accuracy.

Evaluating the impact of a test strategy that substantially changes diagnostic and treatment pathways, potentially leading to increased access to testing and subsequent healthcare is challenging. A primary assumption made in the all the decision models considered is that the hypothetical cohort of patients in the model can all follow each of the strategies being compared. In reality this is unlikely to be the case when a POCT is introduced, particularly when the POCT allows testing in a different healthcare setting. For example, the models considering testing for malaria typically compare strategies of treatment based on results of

POCT with a strategy of treatment based on microscopy (laboratory) testing. They do not include patients who in reality would receive a POCT if available, but could never have access to microscopy – who potentially would receive either empirical treatment or no treatment at all. Future models could consider incorporation of comparative strategies which include a realistic mixture of alternative pathways.

We believe that there are two main reasons why the omissions in economic evaluations for POCTs described in our review occur. First, there is lack of awareness of the routes by which tests impact on patients beyond test accuracy. Many courses, guides and textbooks on test evaluation solely focus on sensitivity, specificity and other measures of test accuracy. Recently a framework of mechanisms by which tests impact on patients was published based on a review of over 100 clinical testing scenarios evaluated in randomised controlled trials (101). The framework identified issues related to testing timeframes as key mechanisms for creating patient benefit, alongside accurate and confident decision-making, and reducing the direct harms of testing. We would recommend using the checklist that accompanies this framework when scoping models for test scenarios. Second are the challenges in obtaining estimates of the parameters required to create a decision model that factors in the impact of changing time frames and setting on patient outcomes and costs. There may often be a lack of empirical evidence upon which to base parameter estimates, while expert judgement and sensitivity analyses may also be required. As a minimum, authors should acknowledge the limitations of their models and simplifications that have been made where they do not fully represent the reality of how POCTs impact on patients and costs. We have developed a set of considerations that could be consulted during the development of economic models of POCTs (Figure 3). These address key issues we have identified that will enable the development of models that adequately capture both patient related outcomes and cost implications of these technologies. Whilst not all items will be relevant to every test, we hope these will address the inadequacies this review has highlighted.

Extra Considerations When Modelling the Cost-Effectiveness of POCTS

Patient and process related outcomes

Does a difference in test setting or time to diagnosis and treatment impact on:

1. Who will be tested
2. Survival to the start of treatment
3. The health state at the start of treatment / disease progression
4. Effectiveness of treatment (e.g. survival following the initiation of treatment / time to symptom resolution)
5. Psychological harms (e.g. anxiety waiting for results)
6. Time in poor health before treatment
7. Harms of inappropriate treatment
8. Patients lost to follow-up / not commencing treatment
9. Disease spread (infectious diseases only)

Resource use (costs) and changes to the diagnostic pathway

Does using a POCT change:

1. Numbers being tested (e.g. access in resource limited settings)
2. Use of empiric/presumptive therapy
3. Clinician time to administer tests
4. Individuals able to administer tests
5. Number of healthcare consultations (e.g. receipt of results)
6. Logistic requirements for testing, delivery and storage (e.g. refrigeration)
7. Training requirements
8. Costs incurred by patients (e.g. work productivity, transport)

Test characteristics

1. Differences in the number of true positives/false negatives (sensitivity: the percentage with target condition who receive the right diagnosis)
2. Differences in the number of true negatives/false positives (specificity: percentage without target condition who get right diagnosis)

Figure 3 Proposed Considerations During Model Development

There are a number of limitations to the current study. We restricted searches to the last 13 years, and our searches will inevitably have missed some eligible economic evaluations, both those in non-English language journals and those which use different terminology than that included in our electronic search. A database of test names or additional terminology not used in original searches was developed during abstract screening and supplementary

searches were subsequently conducted. However, we would not expect the models we have missed to be qualitatively different than those we have evaluated. It is possible that study reports failed to fully report their models as a consequence of space limitations, and omitted information about pertinent costs or outcomes. We noted relevant information in appendices for some reports suggesting this information may be perceived as less critical to report. A benefit of POCTs unrelated to delay and not investigated in this review is the reduction in secondary tests required. This is an important feature of any new test, improving the testing process for patients and reducing resource use. How POCTs influence the number of tests patients undergo and the cost implications could also be investigated further.

5. Conclusion

This study has shown that many published economic evaluations of POCTs have failed to capture the advantages of increased access and speed to diagnosis and treatment on patient outcomes, and the reductions in patient anxiety and cost that can affect both the health services and patients themselves. We therefore suggest that more should be done to ensure that the methods used in model based economic evaluations of POCTs adequately consider the impact POCTs have on diagnostic and treatment pathways through changes in testing setting and timing.

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Conflict of Interest

The authors have no conflicts of interest to declare.

Web Table 3 Model Inputs Capturing Effect of Time to Diagnosis

Reference	Indication	Impact on patients N=20 (37%)*	Impact on test or treatment costs N=8 (15%)*	Impact on operational costs N=19 (35%)*	Faster testing described in model inputs N=4 (7%)	Perspective of economic evaluation Societal N=4 (14%) Societal/payer N= 2 (7%) Payer N = 23 (79%)
Kip **(41)**	Acute coronary syndrome			Hospitalisation costs**		Societal
Jancovic **(26)**	Acute coronary syndrome		Additional tests **	Hospital referral**		Healthcare payer
Turner **(35)**	Chlamydia and gonorrhoea	Pelvic inflammatory disease Anxiety whilst waiting Harms of presumptive treatment	Pelvic inflammatory disease treatment** Presumptive treatment*	Clinician time** Clinic visits***		Healthcare payer
Schroeder **(33)**	Clostridium difficile infection	Harms of presumptive treatment	Presumptive treatment**	Pre-emptive isolation** Laboratory technician time** Reagents**		Healthcare payer
Fauli **(43)**	Dyspepsia	Symptom free days		Healthcare consultations***		Societal
Nelson **(31)**	Influenza		Empiric treatment** Additional tests**	Laboratory technician time**		Healthcare payer
You **(38)**	Influenza	QALY loss in ICU Illness duration		Clinic visits** ICU utilisation**		Healthcare payer
Alonso **(23)**	Leishmaniasis	Time to treatment initiation		Hospitalisation costs**		Healthcare payer

Reference	Indication	Impact on patients N=20 (37%)*	Impact on test or treatment costs N=8 (15%)*	Impact on operational costs N=19 (35%)*	Faster testing described in model inputs N=4 (7%)	Perspective of economic evaluation Societal N=4 (14%) Societal/payer N= 2 (7%) Payer N = 23 (79%)
Giraldez-Garcia, **(44)**	Pharyngitis	Harms of presumptive treatment	Presumptive treatment**	Clinic visits*** Telephone consultations***		Healthcare payer
Howe **(84)**	Pharyngitis	Time to symptom resolution (QALDs)****		Telephone consultations***		Healthcare payer and societal
Klepser **(28)**	Pharyngitis	Time to symptom resolution (QALDs)****		Telephone consultations***		Healthcare payer
Ward **(36)**	Sepsis	Mortality Earlier resuscitation Disutility of ICU stay		ICU utilisation**		Healthcare payer
Dowdy, Lourenco **(57)**	Tuberculosis	DALYs averted				Healthcare payer
Schnippel, Meyer-Rath **(69)**	Tuberculosis	Appropriate treatment Loss to follow-up Diagnoses within one week				Healthcare payer
Choi, Miele **(24)**	Tuberculosis	Mortality	Empiric treatment**	Hospitalisation costs**		Healthcare payer
Albert **(83)**	Tuberculosis			Clinic visits***		Healthcare payer
Vassall, Kampen**(65)**	Tuberculosis				Turnaround times for all test strategies reported, but no impact on transmission or mortality assumed	Healthcare payer

Reference	Indication	Impact on patients N=20 (37%)*	Impact on test or treatment costs N=8 (15%)*	Impact on operational costs N=19 (35%)*	Faster testing described in model inputs N=4 (7%)	Perspective of economic evaluation Societal N=4 (14%) Societal/payer N= 2 (7%) Payer N = 23 (79%)
Scherer **(60)**	Tuberculosis			Hospitalisation costs** Patients' loss of income**		Societal
Menzies **(62)**	Tuberculosis	Loss to follow-up				Healthcare payer
Rajalahti **(32)**	Tuberculosis			Inpatient days** Unnecessary isolations**		Healthcare payer
Dowdy **(58)**	Tuberculosis				Time to diagnosis and loss to follow-up reported	Healthcare payer and societal
Dowdy **(20)**	Tuberculosis				Time to diagnosis and loss to follow-up reported	Healthcare payer
Langley **(29)**	Tuberculosis	Time to treatment initiation Loss to follow-up Treatment completion		Clinic visits**	Transmission whilst waiting for treatment initiation not explicitly described	Healthcare payer
Meyer-Rat **(30)**	Tuberculosis	Loss to follow-up		Clinic visits**		Healthcare payer
Khaparade **(27)**	Tuberculosis	Loss to follow-up	Presumptive treatment**			Healthcare payer
Suen **(86)**	Tuberculosis	Time to treatment initiation				Societal

Reference	Indication	Impact on patients N=20 (37%)*	Impact on test or treatment costs N=8 (15%)*	Impact on operational costs N=19 (35%)*	Faster testing described in model inputs N=4 (7%)	Perspective of economic evaluation Societal N=4 (14%) Societal/payer N= 2 (7%) Payer N = 23 (79%)
Tesfaye **(34)**	Tuberculosis	Loss to follow-up Treatment completion Time to treatment initiation		Clinic visits** Clinician time **		Healthcare payer
Oxlade **(85)**	Tuberculosis	Time to treatment initiation				Healthcare payer
You **(37)**	Tuberculosis	Mortality with treatment delay	Presumptive treatment**			Healthcare payer

* Percent of studies where time is relavent **Reduced costs as a result of using POCT ***Increased costs due to slower comparator **** Measured as Quality adjusted life days (QALDs)

Appendix Search Strategies

A1 MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present Search Strategy

1	**Economics/**
2	exp "costs and cost analysis"/
3	Economics, Dental/
4	exp economics, hospital/
5	Economics, Medical/
6	Economics, Nursing/
7	Economics, Pharmaceutical/
8	(economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab.
9	(expenditure$ not energy).ti,ab.
10	value for money.ti,ab.
11	budget$.ti,ab.
12	or/1-11
13	((energy or oxygen) adj cost).ti,ab.
14	(metabolic adj cost).ti,ab.
15	((energy or oxygen) adj expenditure).ti,ab.
16	or/13-15
17	12 not 16
18	("point of care" or "POC test*" or POCT or "near patient" or "desktop technology" or "office laboratory" or "set test*").ti,ab.
19	((test* or diagnos* or assay* or culture* or laborator* or detect* or assess* or identif* or evaluat* or marker* or biomarker*) adj3 (rapid* or quick* or fast* or ancillary* or bedside* or decentralise* or "patient focus*" or portable*)).ti,ab.
20	exp Point-of-Care Systems/
21	18 or 19 or 20
22	17 and 21
23	letter.pt.
24	editorial.pt.
25	23 or 24
26	22 not 25
27	exp animals/ not humans/
28	26 not 27
29	limit 28 to yr="2004-Current"
30	limit 29 to english language

A2 Embase Classic+Embase (via Ovid)

1	Health economics/
2	exp Economic evaluation/
3	exp health care cost/
4	pharmacoeconomics/
5	1 or 2 or 3 or 4
6	(econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab.
7	(expenditure$ not energy).ti,ab.
8	(value adj2 money).ti,ab.
9	budget$.ti,ab.
10	6 or 7 or 8 or 9
11	5 or 10
12	(metabolic adj cost).ti,ab.
13	((energy or oxygen) adj cost).ti,ab.
14	((energy or oxygen) adj expenditure).ti,ab.
15	12 or 13 or 14
16	11 not 15
17	("point of care" or "POC test*" or POCT or "near patient" or "desktop technology" or "office laboratory" or "set test*").ti,ab.
18	((test* or diagnos* or assay* or culture* or laborator* or detect* or assess* or identif* or evaluat* or marker* or biomarker*) adj3 (rapid* or quick* or fast* or ancillary* or bedside* or decentralise* or "patient focus*" or portable*)).ti,ab.
19	exp Point-of-Care Systems/
20	17 or 18 or 19
21	16 and 20
22	letter.pt.
23	editorial.pt.
24	note.pt.
25	22 or 23 or 24
26	21 not 25
27	animal/
28	exp animal experiment/
29	nonhuman/
30	(rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh.
31	27 or 28 or 29 or 30
32	exp human/
33	human experiment/
34	32 or 33
35	31 not (31 and 34)
36	26 not 35
37	conference abstract.pt.
38	36 not 37
39	limit 38 to yr="2004-Current"
40	limit 39 to english language

A3 CINAHL Plus

#	Query	Limiters/Expanders
S29	S23 AND S28	Limiters - Published Date: 20040101-20141231; English Language Search modes - Boolean/Phrase
S28	S24 or S25 or S26 or S27	Search modes - Boolean/Phrase
S27	(MM "Point-of-Care Testing")	Search modes - Boolean/Phrase
S26	AB ((test* or diagnos* or assay* or culture* or laborator* or detect* or assess* or identif* or evaluat*) N3 (rapid* or quick* or fast* or ancillary* or bedside* or decentralise* or "patient focus*" or portable*))	Search modes - Boolean/Phrase
S25	TI ((test* or diagnos* or assay* or culture* or laborator* or detect* or assess* or identif* or evaluat*) N3 (rapid* or quick* or fast* or ancillary* or bedside* or decentralise* or "patient focus*" or portable*))	Search modes - Boolean/Phrase
S24	TI ("point of care" or "POC test*" or POCT or "near patient" or "desktop technology" or "office laboratory" or "set testing") OR AB ("point of care" or "POC test*" or POCT or "near patient" or "desktop technology" or "office laboratory" or "set testing")	Search modes - Boolean/Phrase
S23	S20 not (S21 or S22)	Search modes - Boolean/Phrase
S22	(ZT "doctoral dissertation") or (ZT "masters thesis")	Search modes - Boolean/Phrase
S21	MH "animal studies"	Search modes - Boolean/Phrase
S20	S15 not S19	Search modes - Boolean/Phrase
S19	S16 OR S17 OR S18	Search modes - Boolean/Phrase
S18	PT commentary	Search modes - Boolean/Phrase
S17	PT letter	Search modes - Boolean/Phrase
S16	PT editorial	Search modes - Boolean/Phrase
S15	S13 OR S14	Search modes - Boolean/Phrase
S14	TI (cost or costs or economic* or pharmacoeconomic* or price* or pricing*) OR AB (cost or costs or economic* or pharmacoeconomic* or price* or pricing*)	Search modes - Boolean/Phrase
S13	S9 OR S12	Search modes - Boolean/Phrase
S12	S10 OR S11	Search modes - Boolean/Phrase
S11	MH "health resource utilization"	Search modes - Boolean/Phrase
S10	MH "health resource allocation"	Search modes - Boolean/Phrase
S9	S3 not S8	Search modes - Boolean/Phrase
S8	S4 OR S5 OR S6 OR S7	Search modes - Boolean/Phrase
S7	MH "Business+"	Search modes - Boolean/Phrase
S6	MH "financing, organized+"	Search modes - Boolean/Phrase
S5	MH "financial support+"	Search modes - Boolean/Phrase
S4	MH "Financial management+"	Search modes - Boolean/Phrase
S3	MH "Economics+"	Search modes - Boolean/Phrase
S2	MH "Financial Management+"	Search modes - Boolean/Phrase
S1	MH "Economics+"	Search modes - Boolean/Phrase

A4 PsycINFO

1	"costs and cost analysis"/
2	"cost containment"/
3	(economic adj2 evaluationS).ti,ab.
4	(economic adj2 analy$).ti,ab.
5	(economic adj2 (study or studies)).ti,ab.
6	(cost adj2 evaluation$).ti,ab.
7	(cost adj2 analy$).ti,ab.
8	(cost adj2 (study or studies)).ti,ab.
9	(cost adj2 effective$).ti,ab.
10	(cost adj2 benefit$).ti,ab.
11	(cost adj2 utili$).ti,ab.
12	(cost adj2 minimi$).ti,ab.
13	(cost adj2 consequence$).ti,ab.
14	(cost adj2 comparison$).ti,ab.
15	(cost adj2 identificat$).ti,ab.
16	(pharmacoeconomic$ or pharmaco-economic$).ti,ab.
17	or/1-16
18	(task adj2 cost$).ti,ab,id.
19	(switch$ adj2 cost$).ti,ab,id.
20	(metabolic adj cost).ti,ab,id.
21	((energy or oxygen) adj cost).ti,ab,id.
22	((energy or oxygen) adj expenditure).ti,ab,id.
23	or/18-22
24	(animal or animals or rat or rats or mouse or mice or hamster or hamsters or dog or dogs or cat or cats or bovine or sheep or ovine or pig or pigs).ab,ti,id,de.
25	editorial.dt.
26	letter.dt.
27	dissertation abstract.pt.
28	or/24-27
29	17 not (23 or 28)
30	("point of care" or "POC test*" or POCT or "near patient" or "desktop technology" or "office laboratory" or "set testing").ti,ab.
31	((test* or diagnos* or assay* or culture* or laborator* or detect* or assess* or identif* or

	evaluat*) adj3 (rapid* or quick* or fast* or ancillary* or bedside* or decentralise* or "patient focus*" or portable*)).ti,ab.
32	or/30-31
33	29 and 32
34	limit 33 to yr="2004 -Current"

A5 Health Economic Evaluation Database (HEED) Search Strategy

Abstract	RDT or 'POC test' Or 'POINT-OF-CARE' Or 'POINT-OF-USE' Or 'NEAR-PATIENT' Or 'DESKTOP-TECHNOLOGY' Or POCT
Article title	RDT or 'POC test' Or 'POINT-OF-CARE' Or 'POINT-OF-USE' Or 'NEAR-PATIENT' Or 'DESKTOP-TECHNOLOGY' Or POCT
Abstract	Rapid test within 3
Article title	Rapid test within 3
Abstract	Rapid testing within 3
Article title	Rapid testing within 3
Abstract	Rapid diagnosis within 3
Article title	Rapid diagnosis within 3
Abstract	Rapid diagnostic within 3
Article title	Rapid diagnostic within 3
Abstract	Rapid culture within 3
Article title	Rapid culture within 3
Abstract	Rapid assay within 3
Article title	Rapid assay within 3
Abstract	Rapid detect within 3
Article title	Rapid detect within 3
Abstract	Rapid identification within 3
Article title	Rapid identification within 3
Article title	Rapid identify within 3
Abstract	Rapid identify within 3
Abstract	Rapid evaluation within 3
Article title	Rapid evaluation within 3
Abstract	Fast test within 3
Article title	Fast test within 3
Abstract	Fast testing within 3
Article title	Fast testing within 3
Abstract	Fast diagnosis within 3
Article title	Fast diagnosis within 3
Abstract	Fast diagnostic within 3
Article title	Fast diagnostic within 3
Abstract	Fast culture within 3

Article title	Fast culture within 3
Abstract	Fast assay within 3
Article title	Fast assay within 3
Abstract	Fast detect within 3
Article title	Fast detect within 3
Abstract	Fast identification within 3
Article title	Fast identification within 3
Article title	Fast identify within 3
Abstract	Fast identify within 3
Abstract	Fast evaluation within 3
Article title	Fast evaluation within 3
Abstract	Quick test within 3
Article title	Quick test within 3
Abstract	Quick testing within 3
Article title	Quick testing within 3
Abstract	Quick diagnosis within 3
Article title	Quick diagnosis within 3
Abstract	Quick diagnostic within 3
Article title	Quick diagnostic within 3
Abstract	Quick culture within 3
Article title	Quick culture within 3
Abstract	Quick assay within 3
Article title	Quick assay within 3
Abstract	Quick detect within 3
Article title	Quick detect within 3
Abstract	Quick identification within 3
Article title	Quick identification within 3
Article title	Quick identify within 3
Abstract	Quick identify within 3
Abstract	Quick evaluation within 3
Article title	Quick evaluation within 3

A6 NHS Economic Evaluation Database (EED) Search Strategy

#1	("point of care" or "POC test*" or POCT or "near patient" or "desktop technology" or "office laboratory" or "set testing"):ti,ab,kw
#2	((test* or diagnos* or assay* or culture* or laborator* or detect* or assess* or identif* or evaluat*) near/3 (rapid* or quick* or fast* or ancillary* or bedside* or decentralise* or "patient focus*" or portable*))
#3	MeSH descriptor: [Point-of-Care Systems] explode all trees
#4	#1 or #2 or #3
#5	#4 in Economic Evaluations (Word variations have been searched)
#6	#5 Publication Year from 2004 to 2014 (Word variations have been searched)

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